



# Daily Chlorhexidine Bathing in General Hospital Units – Results of the ABATE Infection Trial (Active BATHing to Eliminate Infection)

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#### 998. Utility of Routine Genomic Sequencing for Infection Control Surveillance

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**Session:** 134. Where Did That Come From? Transmission Risks in Healthcare  
Friday, October 6, 2017: 10:30 AM

**Background.** Recent work indicates that comprehensive genomic sequencing can be a highly effective tool in defining the transmission of microbial pathogens. We have studied the utility of the routine use of genomic sequencing for infection control surveillance in an academic medical center.

**Methods.** The genomes of inpatient and emergency department isolates of *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Klebsiella pneumoniae*, and *Enterococcus faecium* were sequenced. Within each species, single-nucleotide polymorphisms (SNP) were identified in the core genome for all isolates using alignment-based methods. The number of SNP differences between isolate pairs was determined and used, in combination with the patient's electronic medical records to identify potential transmission events.

**Results.** Between September 2016 and March 2017, 388 *S. aureus*, 66 *P. aeruginosa*, 48 *K. pneumoniae*, and 29 *E. faecium* isolates were sequenced from 373 patients. There was variation in the distribution of SNP differences between inpatient isolates for the four pathogens; with the least variability for *E. faecium* and greatest for *P. aeruginosa*. The majority of the bacterial isolates from separate patients appeared to be genetically unique exhibiting marked SNP differences from other isolates. There were 19 sets of isolates where the SNP variation between interpatient isolates was either comparable to that of inpatient variation (12) and suggestive of recent transmission events, or with SNP variation somewhat greater than the inpatient SNP variation (7) suggesting relative relatedness. Only one of the highly related sets had been previously identified by standard infection control surveillance. Likely transmissions appeared to have occurred both in the inpatient and outpatient settings, and the transmission routes were not always apparent.

**Conclusion.** The routine use of genomic sequencing analysis identified previously unrecognized likely transmission events within the institution's patient population that are of relevance to infection control surveillance. This capacity should significantly enhance our understanding of the epidemiology of hospital acquired infections, and assist in developing and implementing new prevention strategies.

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#### 999. Invasive *Mycobacterium abscessus* Infection after Cardiac Surgery: Epidemiology and Clinical Outcomes

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**Session:** 134. Where Did That Come From? Transmission Risks in Healthcare  
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**Background.** We recently mitigated a clonal outbreak of *Mycobacterium abscessus*, including a large cluster of patients who developed invasive infection after exposure to heater-cooler units (HCU) during cardiac surgery. Recent studies have described a small number of *Mycobacterium chimaera* infections linked to open-heart surgery; however, little is known about the epidemiology and clinical courses of cardiac surgery patients with invasive infection from rapidly-growing mycobacteria, such as *M. abscessus*.

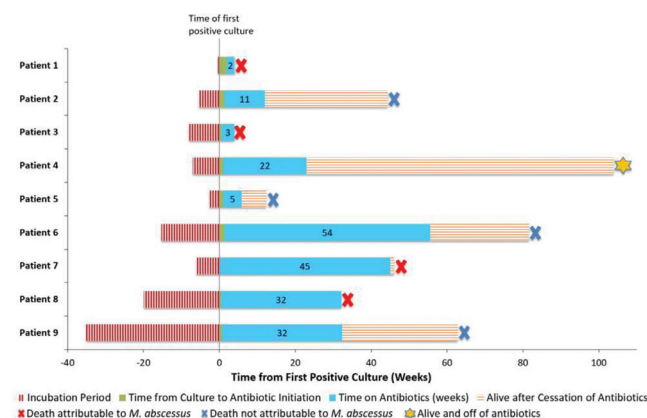
**Methods.** We retrospectively collected clinical data from all patients who underwent cardiac surgery at our hospital and had positive cultures for *M. abscessus* from 2013 to 2016. We excluded heart transplant recipients and patients who at time of diagnosis had ventricular assist devices. We analyzed patient characteristics, antibiotic treatment courses, surgical interventions, and clinical outcomes.

**Results.** Nine cardiac surgery patients who met the case definition developed culture-proven invasive infection from *M. abscessus* (Figure 1). Seven (78%) infections occurred after surgeries that included valve replacement. Median time from suspected inoculation in the operating room to first positive culture was 49 days

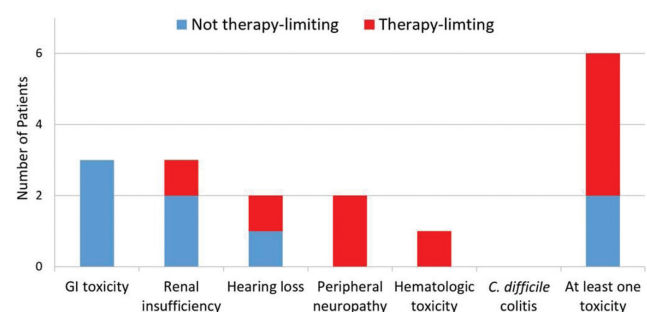
(interquartile range, 38–115 days). Seven (78%) patients had bloodstream infections, and six (67%) patients had sternal wound infections. Six (67%) patients developed disseminated disease with infection at multiple sites. All patients received combination antimicrobial therapy. The most common majority regimen ( $n = 6$ ) was imipenem, amikacin, and tigecycline. Four (44%) patients experienced therapy-limiting antibiotic toxicities (Figure 2). Seven (78%) patients were well enough to undergo at least one surgical debridement. Five (56%) patients stopped therapy due to presumed cure, but four (44%) patients had deaths attributable to *M. abscessus* infection.

**Conclusion.** Invasive *M. abscessus* infection after cardiac surgery was associated with high morbidity and mortality. Most patients underwent surgical debridement and received prolonged three-drug antimicrobial therapy, which was complicated by numerous antibiotic toxicities. Treatment cured five patients, but four patients died from mycobacterial disease.

**Figure 1.** Clinical courses of 9 patients who developed invasive *Mycobacterium abscessus* infection after cardiac surgery. Incubation period is given from time of suspected inoculation in operating room to time that the first positive culture was obtained.



**Figure 2.** Antibiotic toxicities experienced by 9 cardiac surgery patients treated for invasive *Mycobacterium abscessus* infection. 4 of 6 patients with toxicities required a change in antibiotic regimen.



**Disclosures.** All authors: No reported disclosures.

#### 1000. Daily Chlorhexidine Bathing in General Hospital Units – Results of the ABATE Infection Trial (Active BATHing to Eliminate Infection)

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**Session:** 134. Where Did That Come From? Transmission Risks in Healthcare  
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**Background.** Universal decolonization with daily chlorhexidine (CHG) bathing with and without nasal decolonization has significantly reduced positive MRSA clinical cultures and bloodstream infections in adult ICUs in several clinical trials. We

evaluated whether decolonization was similarly effective in a lower risk hospitalized population.

**Methods.** We conducted a 2 arm cluster-randomized trial involving a 1-year baseline period (April 2013–March 2014) and a 21-month intervention period (June 2014–February 2016). All noncritical care units in a hospital were assigned to the same strategy. These were (1) Routine Care: routine bathing product and frequency and (2) Decolonization: CHG for routine daily bathing (2% leave-on CHG) or showering (4% rinse-off CHG) for all patients plus mupirocin for 5 days for known MRSA. Universal ICU decolonization was in place in both arms by September 2013. Differences between the arms in the outcome rates between the baseline and intervention periods were assessed with proportional hazards models, using shared frailties to account for clustering by hospital. The primary analysis was as-randomized and unadjusted. Primary outcome was any MRSA or VRE clinical isolate attributable to the unit. Secondary outcome was all-cause bloodstream infections. Additional analyses adjusted for age, gender, race, Medicaid insurer, surgery, and comorbidities.

**Results.** We randomized 53 hospitals in 15 states. There were 194 adult units with 189,616 admissions in the baseline period and 340,350 in the intervention period. Common unit types included mixed medical surgical (30%), cardiac (20%), step-down (11%), medical (10%), surgical (10%), and oncology (4%). There were no significant differences between arms in the relative hazards for intervention vs. baseline for either outcome (Table and Figure). Adjusted analyses yielded similar results.

**Table 1. Event Rates and Model Results for the ABATE Infection Trial**

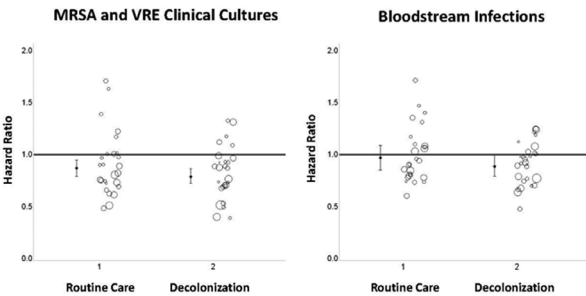
Strategy	PRIMARY OUTCOME Unit-Attributable MRSA+VRE Clinical Cultures			
	Baseline <sup>1</sup>	Intervention <sup>1</sup>	HR <sup>2</sup>	P-value <sup>3</sup>
Routine Care	2.4	2.1	0.87 (0.79-0.95)	0.16
Decolonization	2.2	1.7	0.79 (0.73-0.87)	
	SECONDARY OUTCOME Unit-Attributable Bloodstream Infections			
	Baseline <sup>1</sup>	Intervention <sup>1</sup>	HR <sup>2</sup>	P-value <sup>3</sup>
Routine Care	1.3	1.3	0.97 (0.86-1.09)	0.35
Decolonization	1.3	1.2	0.89 (0.80-1.00)	

<sup>1</sup>Events per 1,000 patients

<sup>2</sup>HR = Hazard Ratio from unadjusted proportional hazard model analyses; model estimates are not

equal to ratio of raw risk due to differential length-of-stay and effect of clustering within hospital

<sup>3</sup>P-value for the null hypothesis that the hazard ratio in each treatment arm is equal



**Figure 1.** Group-specific hazard ratios (HR) and 95% confidence intervals (vertical lines) for trial outcomes. Bubble plots of HRs from individual hospitals relative to their group effects are shown. Bubble size indicates relative number of patients contributing data.

**Conclusion.** Universal daily CHG bathing or showering plus targeted mupirocin for MRSA+ patients in non-critical care units did not reduce the combination of positive MRSA and VRE clinical cultures or bloodstream infections due to all pathogens. Further analyses to assess for any differential effects in high-risk subpopulations will be important.

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#### 1001. A Single Dose Monoclonal Antibody (mAb) Immunoprophylaxis Strategy to Prevent RSV Disease in All Infants: Results of the First in Infant Study with MEDI8897

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Session: 135. PIDS Featured Abstracts

Friday, October 6, 2017: 10:30 AM

**Background.** RSV is the most common cause of lower respiratory tract infection (LRTI) among infants making prevention of RSV disease a public health priority. A significant unmet need exists for RSV prevention in healthy infants. Our goal is to develop a mAb with an extended half-life ( $t_{1/2}$ ) capable of protecting infants for an entire RSV season by using a single intramuscular (IM) dose. This study was conducted to evaluate the safety profile, pharmacokinetics (PK), RSV neutralizing antibody titers, and anti-drug antibody (ADA) responses for MEDI8897 in healthy preterm infants born between 32 and 35 weeks gestational age.

**Methods.** Infants were randomized 4:1 to receive a single IM injection of MEDI8897 10 mg ( $n = 8$ ), 25 mg ( $n = 31$ ), 50 mg ( $n = 32$ ) or placebo ( $n = 18$ ) and followed for 360 days. Enrollment occurred during the 2015 RSV seasons in the US, South Africa, and Chile. Blood was collected at multiple timepoints. Infants who met criteria for a medically-attended (MA) LRTI had nasal swabs obtained for RSV testing by RT-PCR.

**Results.** A total of 85/89 (95.5%) infants completed the study. Adverse events (AEs) were reported in 17/18 (94.4%) placebo and 66/71 (93.0%) MEDI8897 recipients. Five serious AEs (three LRTIs, two febrile seizures) were reported in three MEDI8897 recipients. No events were consistent with hypersensitivity reactions. The estimated MEDI8897 serum  $t_{1/2}$  ranged from 62.5 to 72.9 days. On day 151, 87% of the infants who received the 50 mg dose of MEDI8897 had serum concentrations above the target  $EC_{50}$  level of 6.8  $\mu$ g/ml, and 93.3% showed a  $\geq 3$ -fold rise from baseline in serum anti-RSV neutralizing antibody titers. ADA was detected in 28.2% of MEDI8897 recipients, but when present was not associated with any safety findings. ADA was detected at day 361 only in 26.5% of subjects. MA-LRTI was reported in 5 (7%) MEDI8897 recipients through 150 days after dosing. The one subject with an MA-LRTI caused by RSV had received a 10 mg dose of MEDI8897.

**Conclusion.** In healthy preterm infants, the safety profile of MEDI8897 was favorable. The extended  $t_{1/2}$  of MEDI8897 with the corresponding increase in RSV neutralizing antibody levels was confirmed and supports protection from RSV disease during a typical 5-month season with a single 50 mg IM dose.

This study was sponsored by MedImmune.

**Disclosures.** J. B. Domachowski, MedImmune: Investigator, Research grant; Regeneron: Investigator, Research grant; Pfizer: Investigator, Research grant; Glaxo Smith Kline: Investigator, Research grant; Novavax: Investigator, Research grant; Janssen: Investigator, Research grant; A. Khan, MedImmune: Employee and Shareholder, Salary and stock; M. T. Esser, MedImmune: Employee and Shareholder, Salary and stock; K. M. Jensen, MedImmune: Employee and Shareholder, Salary and stock; T. Takas, MedImmune: Employee and Shareholder, Salary and stock; T. Villafana, MedImmune: Employee and Shareholder, Salary and stock; F. Dubovsky, MedImmune: Employee and Shareholder, Salary and stock; M. P. Griffin, MedImmune: Employee and Shareholder, Salary and stock

#### 1002. Respiratory Syncytial Virus bronchiolitis: Impact of second-hand smoke exposure on immune profiles

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Session: 135. PIDS Featured Abstracts

Friday, October 6, 2017: 10:30 AM

**Background.** RSV is the leading cause of hospitalization for bronchiolitis in infants and young children worldwide. Second-hand smoke (SHS) exposure has been associated with increased morbidity in children with respiratory infections. The

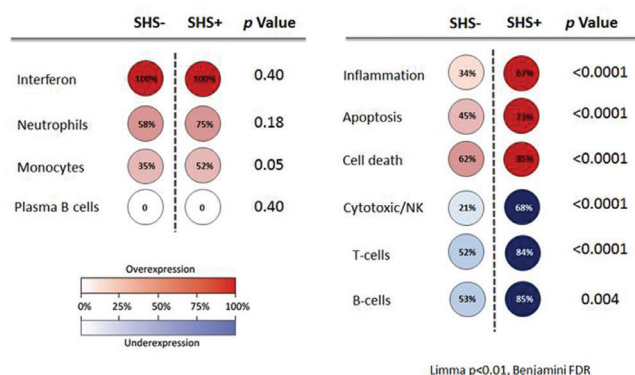
objectives of this study were to explore the association between SHS measured by hair nicotine and disease severity in infants with RSV infection, and to define its impact on the blood transcriptional immune profiles.

**Methods.** Single-center, prospective study of previously healthy infants presenting to the Emergency Department with RSV bronchiolitis with and without SHS exposure assessed by hair nicotine levels. Exclusion criteria included: prematurity; chronic medical conditions, and insufficient hair. Clinical outcomes were assessed using a clinical disease severity score (CDSS; ranging from 0 to 15) and care provided (hospitalization and intensive care). Blood samples from patients and healthy controls were obtained at enrollment for gene expression profiling, and differences in profiles stratified by SHS exposure.

**Results.** A total of 70 infants with RSV were enrolled (median age 2.7 months; 44 (62.8%) males; 44 (62.8%) white). Hair nicotine was detected in 45 (64.2%) infants with RSV while 25 RSV+ infants had undetectable hair nicotine levels. Demographic variables were not significantly different between SHS exposed and nonexposed infants. Median nicotine concentrations in infants with severe (CDSS >10) vs. mild RSV disease (CDSS < 5) were 5.3 and 2.1 ng/mg ( $P = 0.49$ ). In addition, blood transcriptional profiles in RSV infants exposed to SHS vs. nonexposed, were characterized by significantly greater overexpression of genes related to inflammation, apoptosis and cell death, and greater suppression of T and B cell-related genes (Figure 1).

**Conclusion.** In otherwise healthy infants with RSV infection exposure to SHS was associated with greater inflammation and blunted T and B cell responses. Although not statistically significant, hair nicotine levels were higher in patients with more severe RSV bronchiolitis.

#### Gene expression between SHS exposed and non exposed infants



**Disclosures.** O. Ramilo, Abbvie: Board Member, Consulting fee; Regeneron: Board Member, Consulting fee; Janssen: Board Member and Investigator, Consulting fee and Research grant; NIH: Grant Investigator, Research grant; A. Mejias, Janssen: Investigator and Scientific Advisor, Consulting fee and Research support; Abbvie: Consultant and Scientific Advisor, Speaker honorarium; Novartis: CME lecture, Speaker honorarium; NIH: Investigator, Research grant

#### 1684. Obesity Following Antiretroviral Therapy (ART) Initiation is Common and Influenced by Both Traditional and HIV-/ART-Specific Risk Factors

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Session: 188. HIV: Modern ART

Friday, October 6, 2017: 2:00 PM

**Background.** Weight gain commonly occurs among HIV-infected (HIV+) adults initiating modern ART regimens, and obesity is increasingly reported in this population. However, data regarding specific risk factors for obesity development after ART initiation are conflicting.

**Methods.** We retrospectively analyzed data from a cohort of HIV+ adults who initiated ART between January 1, 2000 and December 31, 2015 in Rio de Janeiro, Brazil. Body mass index (BMI) was assessed at ART initiation. Participants who were non-obese (BMI < 30 kg/m<sup>2</sup>) at baseline and had  $\geq 90$  days of ART exposure were followed for development of obesity. Participants were censored at the time of obesity diagnosis or at end of follow-up (defined as death, loss to follow-up, end of study period or 2 years after their last weight measurement). Incidence rates were estimated using Poisson regression models and risk factor assessment was calculated using Cox regression models accounting for death and loss to follow-up as competing risks.

**Results.** Participants ( $n = 1,794$ ) were 61.3% male, 48.3% white and had a median age of 36.3 years. At ART initiation, participants had a median BMI of 22.6 kg/m<sup>2</sup> and BMI category distribution was: underweight 14%, normal weight 56%, overweight 22% and obese 8%. Of the 1,567 non-obese participants followed after ART initiation, 76% gained weight, 44% increased their BMI category and 18% developed obesity. Median